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B. Webb
6/15/01

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Typed or Printed Name	Donna Macedo		
Signature	Donna Macedo	**Date**	May 29, 2001

AMENDMENT		
Address to: Commissioner for Patents Washington, D.C. 20231	Attorney Docket Confirmation No.	CLON015
	First Named Inventor	Chenchik et al.
	Application Number	09/440,829
	Filing Date	November 15, 1999
	Group Art Unit	1655
	Examiner Name	Forman, B.
	Title	*Long Oligonucleotide Arrays*

Sir:

This amendment is submitted in response to the First Office Action dated December 29, 2000.

Please amend the above identified application as follows:

IN THE SPECIFICATION

Please replace the paragraph beginning on page 41, line 1, with the following rewritten paragraph:

TABLE 1

Array Position	Probe Name	Probe Sequence
A1	s64_2	AC CTAGAAAGCT ATTTGAGCTG GATCCGTCCC TCTGATCGTG ACGCCTTCCT TGAAGAATTT CGGACATCTC TGCCAAAGTC TTGTGACCTG TAGCTGCCA (SEQ ID NO:3)
A2	s64_2_90	AGAAAGCTATTTGAGCTGGATCCGTCCCTCTGATCGTGACGCCTTCCTTGAAGAATTTCGGACATCTCTGCCAAAGTCTTGTGACCTGTA (SEQ ID NO:4)
A3	s64 2 80	AGCTATTTGAGCTGGATCCGTCCCTCTGATCGTGACGCCTTCCTTGAAGAATTTCGGACATCTCTGCCAAAGTCTTGTGA (SEQ ID NO:5)
A4	s64 2 70	ATTTGAGCTGGATCCGTCCCTCTGATCGTGACGCCTTCCTTGAAGAATTTCGGACATCTCTGCCAAAGTA (SEQ ID NO:6)
B1	s64 2 60	AGCTGGATCCGTCCCTCTGATCGTGACGCCTTCCTTGAAGAATTTCGGACATCTCTGCCA (SEQ ID NO:7)
B2	s64 2 50	AATCCGTCCCTCTGATCGTGACGCCTTCCTTGAAGAATTTCGGACATCTA (SEQ ID NO:8)
C1	s26 2	AAACCCAGGA AAATACCAAA TCCAGATTTC TTTGAAGATC TGGAACCTTT CAGAATGACT CCTTTTAGTG CTATTGGTTT GGAGCTGTGG TCCATGACCTA (SEQ ID NO:9)
C2	s26_2_90	AGGAAAATACCAAATCCAGATTTCTTTGAAGATCTGGAACCTTTCAGAATGACTCCTTTTAGTGCTATTGGTTTGGAGCTGTGGTCCATA (SEQ ID NO:10)
C3	s26 2 80	AATACCAAATCCAGATTTCTTTGAAGATCTGGAACCTTTCAGAATGACTCCTTTTAGTGCTATTGGTTTGGAGCTGTGGA (SEQ ID NO:11)
C4	s26 2 70	AAAATCCAGATTTCTTTGAAGATCTGGAACCTTTCAGAATGACTCCTTTTAGTGCTATTGGTTTGGAGCA (SEQ ID NO:12)
D1	s26 2 60	ACAGATTTCTTTGAAGATCTGGAACCTTTCAGAATGACTCCTTTTAGTGCTATTGGTTTA (SEQ ID NO:13)
D2	s26 2 50	ATTCTTTGAAGATCTGGAACCTTTCAGAATGACTCCTTTTAGTGCTATTA (SEQ ID NO:14)
A5 and E5	c370 2	AGGGTC AGCTGATCTA CGAGTCTGCC ATCACCTGTG AGTACCTGGA TGAAGCATAC CCAGGGAAGA AGCTGTTGCC GGATGACCCC TATGAGAAAG CTTGCA (SEQ ID NO:15)
A6 and E6	c370_2_90	AAGCTGATCTACGAGTCTGCCATCACCTGTGAGTACCTGGATGAAGCATACCCAGGGAAGAAGCTGTTGCCGGATGACCCCTATGAGAAA (SEQ ID NO:16)
A7 and E7	c370 2 80	AATCTACGAGTCTGCCATCACCTGTGAGTACCTGGATGAAGCATACCCAGGGAAGAAGCTGTTGCCGGATGACCCCTATA (SEQ ID NO:17)
A8 and E8	c370 2 70	ACGAGTCTGCCATCACCTGTGAGTACCTGGATGAAGCATACCCAGGGAAGAAGCTGTTGCCGGATGACCA (SEQ ID NO:18)
B5 and F5	c370 2 60	ACTGCCATCACCTGTGAGTACCTGGATGAAGCATACCCAGGGAAGAAGCTGTTGCCGGAA (SEQ ID NO:19)
B6 and F6	c370 2 50	AATCACCTGTGAGTACCTGGATGAAGCATACCCAGGGAAGAAGCTGTTGA (SEQ ID NO:20)
G1	s91 3	AGGCCCCAAAT GGCTGGAAAT CTCGCCTATT TAGGCATTCT ACTCAGAAAA ACCTTAAAAA TTCACAAATG TGTCAGAAGA GCCTTGATGT GGAAACCGATA (SEQ ID NO:21)
G2	s91_3_90	ACAAATGGCTGGAAATCTCGCCTATTTAGGCATTCTACTCAGAAAAACCTTAAAAATTCACAAATGTGTCAGAAGAGCCTTGATGTGGAA (SEQ ID NO:22)

G3	s91 3 80	AGGCTGGAAATCTCGCCTATTTAGGCATTCTACTCAGAAAAACCTTAAAAATTCACAAATGTGTCAGAAGAGCCTTGATA (SEQ ID NO:23)
G4	s91 3 70	AGAAATCTCGCCTATTTAGGCATTCTACTCAGAAAAACCTTAAAAATTCACAAATGTGTCAGAAGAGCCA (SEQ ID NO:24)

Please replace the paragraph beginning on page 42, line 1, with the following rewritten paragraph:

H1	s91 3 60	ACTCGCCTATTTAGGCATTCTACTCAGAAAAACCTTAAAAATTCACAAATGTGTCAGAAA (SEQ ID NO:25)
H2	s91 3 50	ACTATTTAGGCATTCTACTCAGAAAAACCTTAAAAATTCACAAATGTGTA (SEQ ID NO:26)
E1	s97 4	ATAGGAGGGG TGAAGCCCAG CTGCTCATGA ACGAGTTTGA GTCAGCCAAG GGTGACTTTG AGAAAGTGCT GGAAGTAAAC CCCCAGAATA AGGCTGCAAGA (SEQ IDNO:27)
E2	s97_4_90	AGGGGTGAAGCCCAGCTGCTCATGAACGAGTTTGAGTCAGCCAAGGGTGACTTTGAGAAAGTGCTGGAAGTAAACCCCCAGAATAAGGCA (SEQ ID NO:28)
E3	s97 4 80	AGAAGCCCAGCTGCTCATGAACGAGTTTGAGTCAGCCAAGGGTGACTTTGAGAAAGTGCTGGAAGTAAACCCCCAGAATA (SEQ ID NO:29)
E4	s97 4 70	ACCAGCTGCTCATGAACGAGTTTGAGTCAGCCAAGGGTGACTTTGAGAAAGTGCTGGAAGTAAACCCCCA (SEQ ID NO:30)
F1	s97 4 60	ATGCTCATGAACGAGTTTGAGTCAGCCAAGGGTGACTTTGAGAAAGTGCTGGAAGTAAAA (SEQ ID NO:31)
F2	s97 4 50	AATGAACGAGTTTGAGTCAGCCAAGGGTGACTTTGAGAAAGTGCTGGAAA (SEQ ID NO:32)
C5	s74 3	ATATGT AACTGAAGAA GGTGACAGTC CTTTGGGTGA CCATGTGGGT TCTCTGTCAG AGAAATTAGC AGCAGTCGTC AATAACCTAA ATACTGGGCA AGTGTA (SEQ ID NO:33)
C6	s74_3_90	AAACTGAAGAAGGTGACAGTCCTTTGGGTGACCATGTGGGTTCTCTGTCAGAGAAATTAGCAGCAGTCGTCAATAACCTAAATACTGGGA (SEQ IDNO:34)
C7	s74 3 80	AAAGAAGGTGACAGTCCTTTGGGTGACCATGTGGGTTCTCTGTCAGAGAAATTAGCAGCAGTCGTCAATAACCTAAATAA (SEQ ID NO:35)
C8	s74 3 70	AAGTGACAGTCCTTTGGGTGACCATGTGGGTTCTCTGTCAGAGAAATTAGCAGCAGTCGTCAATAACCTA (SEQ ID NO:36)
D5	s74 3 60	ACAGTCCTTTGGGTGACCATGTGGGTTCTCTGTCAGAGAAATTAGCAGCAGTCGTCAATA (SEQ ID NO:37)
D6	s74 3 50	ACTTTGGGTGACCATGTGGGTTCTCTGTCAGAGAAATTAGCAGCAGTCGA (SEQ IDNO:38)

TABLE 1 (CONT)

In the claims:

1. (Once Amended) An array comprising at least one pattern of probe oligonucleotide spots stably associated with the surface of a solid support, wherein each probe oligonucleotide spot of said pattern comprises an oligonucleotide probe composition made up of long oligonucleotide probes that range in length from about 50 to 120 nucleotides.

3. (Once Amended) The array according to Claim 2, wherein each probe oligonucleotide spot in said pattern hybridizes to a different target nucleic acid.

Cancel Claim 4.

Cancel Claim 5.

Cancel Claim 6.

10. (Once Amended) The array according to Claim 1, wherein the spots on said array do not exceed a density of about $1000/cm^2$.

11. (Once Amended) The array according to Claim 10, wherein the spots on said array do not exceed a density of about $400/cm^2$.

12. (Once Amended) The array according to Claim 1, wherein the spots on said array range from about 50 to 50,000 in number.

13. (Once Amended) The array according to Claim 1, wherein the spots on said array range from about 50 to 10,000 in number.

14. (Once Amended) An array comprising a pattern of probe oligonucleotide spots covalently bound to the surface of a solid support, wherein each probe oligonucleotide spot comprises a long oligonucleotide probe composition made up of long oligonucleotides of from about 60 to 100 nucleotides in length.

16. (Once Amended) The array according to Claim 15, wherein each probe oligonucleotide spot in said pattern hybridizes to a different target nucleic acid.

17. (Once Amended) The array according to Claim 15, wherein two or more probe oligonucleotide spots in said pattern hybridize to the same target nucleic acid.

18. (Once Amended) The array according to Claim 14, wherein each of said unique oligonucleotides ranges from about 65 to 90 nucleotides in length.

19. (Once Amended) The array according to Claim 14, wherein the spots on said array do not exceed a density of about $1000/cm^2$.

20. (Once Amended) The array according to Claim 14, wherein the spots on said array do not exceed a density of about $400/cm^2$.

21. (Once Amended) The array according to Claim 14, wherein the spots on said array range from about 50 to 50,000 in number.

22. (Once Amended) The array according to Claim 14, wherein the spots on said array range from about 50 to 10,000 in number.

23. (Once Amended) An array comprising a pattern of probe oligonucleotide spots of a density that does not exceed about 400 spots/cm^2 covalently attached to the surface of a glass

support, wherein each probe oligonucleotide spot comprises an oligonucleotide probe composition made up of long oligonucleotides of from about 65 to 90 nucleotides in length.

Please add the following new claims:

--36. The array according to Claim 1, wherein any variance in hybridization efficiency among any to probes of said array does not exceed about 10-fold.

37. The array according to Claim 14, wherein any variance in hybridization efficiency among any to probes of said array does not exceed about 10-fold.

38. The array according to Claim 23, wherein any variance in hybridization efficiency among any to probes of said array does not exceed about 10-fold. --

REMARKS

In view of the above amendments and the following remarks, the Examiner is respectfully requested to withdraw the rejections and allow Claims 1-3, 7-23 and 35, as well as newly added Claims 36-38, the only claims pending and currently under examination in this application.

The undersigned thanks the Examiner for her time during the helpful interview that was held on April 19, 2001. During the interview the subject invention was discussed with respect to the cited Brown reference, specifically with respect to whether Brown anticipates the claims that require a specific length range for the probe oligonucleotides.

The specification has been amended to include the requisite SEQ ID numbers.

The Claims have been amended to replace abbreviations with the full word, remove the terminology "corresponds" and to rearrange wording to provide clearer antecedent basis. As such, the above amendments introduce no new matter to the application and their entry by the Examiner is respectfully requested.

Attached hereto is a marked up version of the changes made to the claims by the current amendment. The attached page is captioned **"Version with markings to show changes made."**

Claims 1-23 and 35 were rejected under 35 U.S.C. §112, 2nd ¶ for a number of asserted reasons, each of which is addressed below:

a. With respect to this issue, the claims have been amended to spell out "nucleotide."

b. The Applicants respectfully submit that the term "spot" is not indefinite to one of skill in the art when read in light of the specification because this term is extensively defined in the specification at page 11, line 27 to page 12, line 20.

c. The Applicants respectfully submit that the term "stably associated" is not indefinite to one of skill in the art when read in light of the specification because this term is extensively defined in the specification at page 13, lines 9-25.

d. The phrase "corresponds to a target nucleic acid" has been deleted from the claim and therefore this issued has been addressed.

e. In view of the cancellation of Claims 4 and 6, this issue has been addressed.

f. In view of the cancellation of Claim 5, this issue has been addressed.

g. In view of the cancellation of Claim 6, this issue has been addressed.

h. In view of the cancellation of Claim 6, this issue has been addressed.

i. In view of the adoption of the Examiner's suggestion, this issue has been addressed.

j. In view of the adoption of the Examiner's suggestion, this issue has been addressed.

k. In view of the deletion of the term "corresponds to a target nucleic acid" this issue has been addressed.

l. In view of the deletion of the term in question, this issue has been addressed.

m. In view of the deletion of the term in question, this issue has been addressed.

n. In view of the deletion of the term in question, this issue has been addressed.

o. In view of the replacement of the term "corresponds" with "hybridizes," this issue has been addressed.

p. In view of the adoption of the Examiner's suggestion, this issue has been addressed.

q. In view of the adoption of the Examiner's suggestion, this issue has been addressed.

r. In view of the adoption of the Examiner's suggestion, this issue has been addressed.

s. In view of the deletion of the term in question, this issue has been addressed.

t. In view of the deletion of the term in question, this issue has been addressed.

u. In view of the deletion of the term in question, this issue has been addressed.

v. In view of the deletion of the term in question, this issue has been addressed.

In view of the above remarks and amendments, the Examiner is respectfully requested to withdraw the rejection of Claims 1-23 and 35 under 35 U.S.C. §112, 2nd ¶.

Claims 1-6 & 10-13 have been rejected under 35 U.S.C. § 102(e) as assertedly being anticipated by Brown et al.

In making this rejection, the Examiner points to the passage at Column 13, lines 21 to 25 which reads:

> "Also in a preferred embodiment, the biopolymers are polynucleotides having lengths of at least about 50 bp, i.e., substantially longer than oligonucleotides which can be formed in high density arrays by schemes involving parallel, step-wise polymer synthesis on the array surface."

The Examiner equates the above statement with teaching a range from 50 to 120 nt in length, and therefore concludes that the present claims are anticipated by Brown.

However, it is respectfully submitted that teaching a range of at least about 50 bp is not the same as teaching a range of from 50 to 120 nt. Instead, teaching a range of 50 bp is a much broader range, which literally means at least 50 bp to infinitely long, since there is no upper range in the length that is provided. As such, it is respectfully submitted that the Brown patent at best teaches a very broad range of from 50 bp to infinity.

Therefore, the Brown length range at best "overlaps" with the claimed specific range of the presently claimed invention. Specifically, the claimed specific range of 50 to 120 nt is a small portion of the broad Brown range, in that the upper limit is clearly much smaller than the upper limit of the Brown range, which is infinitely long. As such, the presently claimed range overlaps the Brown range.

Furthermore, Brown fails to provide any specific examples showing an array with probes having a length within the claimed range of the presently claimed invention. In the actual embodiments produced by Brown, the probe length ranges from 250 to 1500 bp in length. See Example 1, Col. 16, line 17. As such, Brown fails to provide specific examples falling within the claimed range of the present claims.

The MPEP specifically addresses the situation where overlapping ranges are present and the cited prior art fails to disclose specific examples falling within the claimed ranges. The MPEP teaches:

> PRIOR ART WHICH TEACHES A RANGE WITHIN, OVERLAPPING, OR TOUCHING THE CLAIMED RANGE ANTICIPATES IF THE PRIOR ART RANGE DISCLOSES THE CLAIMED RANGE WITH "SUFFICIENT SPECIFICITY"

When the prior art discloses a range which touches, overlaps or is within the claimed range, but no specific examples falling within the claimed range are disclosed, a case by case determination must be made as to anticipation. In order to anticipate the claims, the claimed subject matter must be disclosed in the reference with "sufficient specificity to constitute an anticipation under the statute." What constitutes a "sufficient specificity" is fact dependent. If the claims are directed to a narrow range, the reference teaches a broad range, and there is evidence of unexpected results within the claimed narrow range, depending on the other facts of the case, it may be reasonable to conclude that the narrow range is not disclosed with "sufficient specificity" to constitute an anticipation of the claims. The unexpected results may also render the claims unobvious. The question of "sufficient specificity" is similar to that of "clearly envisaging" a species from a generic teaching. See MPEP Section 2131.02 . A 35 U.S.C. 102/103 combination rejection is permitted if it is unclear if the reference teaches the range with "sufficient specificity." The examiner must, in this case, provide reasons for anticipation as well as a motivational statement regarding obviousness. Ex parte Lee 31 USPQ2d 1105 (Bd. Pat. App. & Inter. 1993) (expanded Board).

MPEP 2131.03

The above guidelines are clearly applicable to the present fact situation, since there are overlapping ranges without specific exemplification within the claimed range in the present situation. As such, the question is whether the Brown disclosure actually discloses the claimed narrow range with "sufficient specificity to constitute an anticipation under the statute."

In the present case, the claimed range is extremely narrow when viewed with respect to Brown's extremely broad range of at least 50 bp, i.e., 50 bp to infinity. In addition, the working exemplification teaches a range of probes of from 250 to 1500 bp. Furthermore, because Brown only teaches producing probes by PCR production protocols, the practical minimal length of a probe that could be produced is at least about 150 bp. As such, the presently claimed narrow range is very narrow with respect to the broad Brown range and well outside the practical ranges and working exemplification taught by Brown.

In addition, the Applicants have found unexpected results when using probes of the claimed narrow ranges, as demonstrated by the enclosed Declaration and reported in the Experimental Section of the application as Example 6.

As such, in the present claims the probe length is a narrow range, Brown teaches a broad range, and the claimed narrow range provides for unexpected results.

The above section of the MPEP teaches that:

If the claims are directed to a narrow range, the reference teaches a broad range, and there is evidence of unexpected results within the claimed narrow range, depending on the other facts of the case, it may be reasonable to conclude that the narrow range is not disclosed with "sufficient specificity" to constitute an anticipation of the claims.

In the present case it is respectfully submitted that the facts of the case, as described above, demonstrate that the claimed narrow is not disclosed with "sufficient specificity" to constitute an anticipation of the claims.

As such, Brown does not anticipate Claims 1-6 & 10-13 under 35 U.S.C. § 102(e) and this rejection may be withdrawn.

Claims 7 and 14-23 have been rejected under 35 U.S.C. §103(a) as obvious over Brown in view of Chetverin. As demonstrated above, Brown fails to teach the narrow claimed range of oligonucleotide length. Furthermore, the narrow claimed range provides for unexpected results. As such, the narrow claimed ranges is not obvious over the Brown disclosure. As Chetverin has been cited solely for its teaching of covalent attachment of the probes to the solid support, Chetverin fails to make up this fundamental deficiency in Brown. As such, Claims 7 and 14-23

are not obvious over the combined teaching of Brown in view of Chetverin and this rejection may be withdrawn.

Claims 8 and 9 have been rejected under 35 U.S.C. §103(a) as obvious over Brown in view of Chetverin and further in view of Graves. As demonstrated above, Brown fails to teach the narrow claimed range of oligonucleotide length. Furthermore, the narrow claimed range provides for unexpected results. As such, the narrow claimed range is not obvious over the Brown disclosure. As Chetverin has been cited solely for its teaching of covalent attachment of the probes to the solid support and Graves has been cited solely for its teaching of cross-linking, these supplemental references fail to make up this fundamental deficiency in Brown. As such, Claims 8 and 9 are not obvious over the combined teaching of Brown in view of Chetverin and Graves and this rejection may be withdrawn.

Claim 9 has been rejected under 35 U.S.C. §103(a) as obvious over Brown in view of Stratagen. As demonstrated above, Brown fails to teach the narrow claimed range of oligonucleotide length. Furthermore, the narrow claimed range provides for unexpected results. As such, the narrow claimed ranges is not obvious over the Brown disclosure. As Stratagene has been cited solely for its teaching of providing reagents in a kit, it fails to make up this fundamental deficiency in Brown. As such, Claim 35 is not obvious over the combined teaching of Brown in view of Stratagene and this rejection may be withdrawn.

Claim 1 was provisionally rejected under 35 U.S.C. § 101 as claiming the same invention as that of Claim 110 of copending application serial no. 09/417,268. Claim 10 of this copending application reads as follows:

> 10. The array according to Claim 1, wherein each of said oligonucleotides ranges from about 15 to 150 nucleotides in length.

Since the array of Claim 10 is dependent on Claim 1, it includes the element that two or more probes hybridize to the same target to produce a complex. See the copending application.

In contrast, Claim 1 of the present application reads as follows:

> 1. An array comprising at least one pattern of probe oligonucleotide spots stably associated with the surface of a solid support, wherein each probe oligonucleotide spot of said pattern comprises an oligonucleotide probe composition made up of long oligonucleotide probes that range in length from about 50 to 120 nucleotides.

Since the element that two or more probes hybridize to the same target to produce a complex present in Claim 10 of the copending application is not present in Claim 1 of present application, the two claims are not claiming the same invention. The Examiner is therefore respectfully requested to withdraw this rejection.

Finally, Claims 1-23 and 35 have been provisionally rejected under the judicially created doctrine of obviousness type double patenting over Claims 1-17 and 53 of copending application No. 09/417,268. In view of the enclosed Terminal Disclaimer, this rejection may be withdrawn.

In view of the above amendments and remarks, this application is considered to be in good and proper form for allowance and the Examiner is respectfully requested to pass this application to issuance. The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815.

Respectfully submitted,
BOZICEVIC, FIELD & FRANCIS LLP

Date: May 29, 2001 By: _____
Bret E. Field
Registration No. 37,620

encs:

- Terminal Disclaimer over U.S. Application Serial No. 09/417,268
- Declaration of Alex Chenchik
- Sequence Listing

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